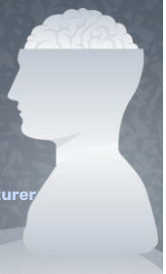
# Behavioral Health: Patients with Severe Depression and Suicidality



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## Learning Objectives

| |
|---|
| Assess the severity of depression in a patient presenting for care. |
| Develop a treatment plan for severe depression. |
| Assess suicidality in a patient presenting for care. |
| Develop a treatment plan for suicidality. |

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01

## Major Depressive Disorder (MDD)

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## Major Depressive Disorder (MDD)

**Also known as**

Depression, major depression, major depressive affective disorder, unipolar depression, unipolar disorder, or unipolar mood disorder.

**Impaired function, increased illness**

Persons with MDD have more pain and physical illness and decreased physical and social functioning.

**Disorder versus "feeling down"**

MDD is different from everyday "ups and downs" that people naturally experience.

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## Evaluation of Depression

- Evaluate functional status, PMH, FH, past treatments (as applicable).
- Screening
- Rule out secondary causes
  - Hypothyroidism, anemia, B-12 deficiency, pain, chronic disease, syphilis.
- Evaluate for suicidality or homicidality
- Additional features (psychosis, seasonal pattern, mixed. etc.)

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## Screening Who should be screened?

- **All patients not receiving treatment for depression**
- Previous recommendations
  - All adults at least every 5 years
  - Part of a health maintenance visit (PHQ-9 in waiting room)
  - High risk groups every year
  - History of depression (PMH)
  - Family history of depression or bipolar disorder
  - Chronic illnesses
  - High utilization of services
  - Pregnancy (2016 recommendation)
  - Those with complaints suggestive of depression (insomnia, fatigue, changes in attention or concentration, etc.)

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## Contributors

When evaluating a patient for MDD, it is essential to rule out underlying medical causes or drug causes

- Cardiovascular
  - Calcium channel blockers, clonidine, methyldopa
  - Beta blockers (controversial)
- Hormones
  - Oral contraceptives (OCAs), corticosteroids, GnRH agonists
- Other
- Acyclovir, Alcohol, AEDs (phenobarbital, primidone, levetiracetam, topiramate), antipsychotics, barbiturates, interferon, isotretinoin, levodopa, varenicline, benzodiazepines, opioids

Celano CM, et al.. Dialogues Clin Neurosci. 2011;13(1):109-25
DSM-5-TR.

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## Screening via PHQ-9

| Over the last 2 weeks, how often have you been bothered by any of the following? | | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|---|
| a | Little interest or pleasure in doing things? | 0 | 1 | 2 | 3 |
| b | Feeling down, depressed, or hopeless? | 0 | 1 | 2 | 3 |
| c | Trouble falling or staying asleep, or sleeping too much? | 0 | 1 | 2 | 3 |
| d | Feeling tired or having little energy? | 0 | 1 | 2 | 3 |
| e | Poor appetite or overeating? | 0 | 1 | 2 | 3 |
| f | Feeling bad about yourself—or that you are a failure or have let yourself or your family down? | 0 | 1 | 2 | 3 |
| g | Trouble concentrating on things, such as reading the newspaper or watching television? | 0 | 1 | 2 | 3 |
| h | Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual? | 0 | 1 | 2 | 3 |
| i | Thoughts that you would be better off dead or of hurting yourself in some way? | 0 | 1 | 2 | 3 |
| For office coding: Total Score =____+____+____+____ | | | | | |

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## Diagnostic Criteria Per DSM-5-TR

Must have **5 features** during the same **2-week period** that **impair functioning:**

1. *Depressed mood (can be an irritable mood in children/adolescents)
2. *Loss of interest or pleasure must be present
3. Weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue
7. Feelings of worthlessness, excessive/inappropriate guilt
8. Decreased concentration
9. Thoughts of death or suicide

DSM-5-TR.

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## Diagnostic Criteria Per DSM-5-TR

- One symptom of either depressed mood or loss of interest or pleasure must be present
- Symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Other medical conditions or substance use must not account for symptoms.
- No history of manic or hypomanic episodes (Bipolar disorder)

DSM-5-TR.

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## 02 Severity Assessment

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## Using the PHQ-9

| | Over the last 2 weeks, how often have you been bothered by any of the following? | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|---|
| a | Little interest or pleasure in doing things? | 0 | 8 | 2 | 3 |
| b | Feeling down, depressed, or hopeless? | 0 | 8 | 2 | 3 |
| c | Trouble falling or staying asleep, or sleeping too much? | 0 | 1 | 2 | 3 |
| d | Feeling tired or having little energy? | 0 | 1 | 2 | 3 |
| e | Poor appetite or overeating? | 0 | 1 | 2 | 3 |
| f | Feeling bad about yourself—or that you are a failure or have let yourself or your family down? | 0 | 1 | 2 | 3 |
| g | Trouble concentrating on things, such as reading the newspaper or watching television? | 0 | 1 | 2 | 3 |
| h | Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual? | 0 | 1 | 2 | 3 |
| i | Thoughts that you would be better off dead or of hurting yourself in some way? | 0 | 1 | 2 | 3 |

For office coding: Total Score = 0 + 4 + 6 + 0 **Total = 10**

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## Test your knowledge

Based on the PHQ-9 score of 10, how would the patient's major depressive disorder (MDD) severity be classified?

A. No MDD
B. Mild
C. Moderate
D. Severe

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## Severity via PHQ-9 Score

| Severity Level | PHQ-9 Total Score | Number of Symptoms According to DSM-5 | Functional Impairment |
|---|---|---|---|
| Mild | 10 – 14 | 5 | Mild |
| Moderate | 15 – 19 | 6 to 7 | Moderate |
| Severe | ≥20 | 8 to 9 | Severe |

**Additional symptoms that indicate severe depression**

- Active suicidal ideation with intent, plan, or attempt
- Active homicidal ideation
- Psychotic symptoms
- Severe anorexia
- Inability to maintain activities of daily living
- Catatonia

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## Treatment Options

## 03

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## Nonpharmacological treatments

- Evidence Based Psychotherapy
  - Recommended for all patients with severe depression
- Repetitive transcranial magnetic stimulation (rTMS)
  - Nonresponse or partial response to 2/+ pharmacotherapies
- Electroconvulsive Therapy (ECT)
  - In severe MDD with at least one of the following:
    - Catatonia, psychosis, severe suicidality,
    - Need for rapid response
    - History of poor response or intolerable SE to multiple antidepressant agents
    - Risk associated with other treatments are greater those associated with MDD
- All patients should be encouraged to eat well, sleep well, and exercise
  - Light therapy and bibliotherapy may be considered

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## Pharmacologic treatments

*Efficacy based on Cipriani A et al. Lancet 2018;391:1357-66

| Treatment option | Efficacy (OR)* | Side effects | Cost | Notes |
|---|---|---|---|---|
| **SSRIs** | 1.52-1.75 | Mild | $ | Considered most tolerable class |
| **SNRIs** | 1.49-1.85 | Moderate | $$ | Helps with pain, +/- energy |
| **Mirtazapine** | 1.89 | Mild | $ | Helps with sleep and appetite |
| **Bupropion** | - | Moderate | $$ | Helps with fatigue |
| **Vortioxetine** | 1.66 | Moderate | $$$ | May help with neuropsychological performance |
| **Vilazodone** | - | Mild | $$$ | "Less" sexual side effects |
| **TCAs** | 1.49-2.13 | High | $ | Helps with pain, insomnia |
| **MAOIs** | - | High | $-$$ | Reserved/last line for TRD |

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## "Newer" treatments

- NMDA antagonists for augmentation
  - Ketamine
    - Can exacerbate psychosis, BP monitoring required.
  - Esketamine
    - Recommended after non-response to several adequate trials
    - Suicidality
- Gepirone
  - Serotonin 1A receptor agonist
    - Note buspirone is a 5HT1A partial agonist and 5HT2 agonist
  - Modest (2.5 point) improvement on HAM-D
  - May be best suited for those with MDD with anxious features

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## Partial or non-response

- Switch
  - Different medication
  - Psychotherapy
- Augment
  - Second generation antipsychotic (SGA)
  - Psychotherapy

**consider degree of response and number of failed trials*

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## Augmenting Agents

- **Antipsychotics**
  - **Aripiprazole, brexpiprazole, cariprazine, lurasidone, quetiapine, olanzapine, or risperidone**
- Antidepressants with alternative MOA
- Lithium
- Liothyronine
- Buspirone
- Stimulants
- Some mood stabilizers (controversial)

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## Test your knowledge

What is an appropriate duration of treatment for severe MDD?

A. 3 months
B. 6 months
C. 9 months
D. Indefinitely

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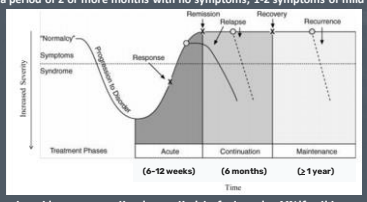
## Duration

**At least 6 months after remission** (Va/DoD 2022)

**Remission = a period of 2 or more months with no symptoms; 1-2 symptoms of mild degree**




**Among patients who achieve response the six-month risk of relapse is ~41% if antidepressants are discontinued**

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## Treatment of Severe Depression

- Psychotherapy should be combined with pharmacotherapy
- When considering medications, efficacy > tolerability
- Consider potent dual mode of action drugs or combinations
  - SNRIs
  - TCAs
  - Vortioxetine
  - MAOIs
- ECT
- Antipsychotic augmentation whether or not psychotic symptoms are present

**VA/DoD. Gautam S et al. Indian J Psychiatry. 2017 Jan;59(Suppl 1):S34-S50.**
**Boyce P et al. Aust Prescr 2021;44:12-15.**

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## Test your knowledge

What limits the use of MAOIs in practice?

A. Side effects
B. Drug interactions
C. Food interactions
D. Administration

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## Aripiprazole versus Bupropion

**Study design**

Systematic literature review of 5 RCTs, which evaluated the efficacy and safety of aripiprazole (ARI-A) or bupropion (BUP-A) augmentation and bupropion switching (BUP-S) for patients with TRD or MDD.

**Data collection**

Including 4480 patients, through April 2023. Outcomes measured were changes in the MADRS, response and remission rates, and serious adverse events.

Ji M, et al. PLoS One. 2024 Apr 26;19(4):e0299020.

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## Results Aripiprazole versus Bupropion

- **ARI-A** was associated with a significantly **higher response rate** compared with **BUP-A** (RR: 1.15; 95% CI: 1.05, 1.25; P = 0.0007; I2 = 23%).
  - Between ARI-A and BUP-A there was no significant difference in improvement of MADRS (WMD: -2.07; 95% CI: -5.84, 1.70; P = 0.28; I2 = 70%)
- **ARI-A** had a significantly **higher remission rate** compared **BUP-S** (RR: 1.22; 95% CI: 1.00, 1.49; P = 0.05; I2 = 59%)
- BUP-A had a significantly higher remission rate compared with BUP-S (RR: 1.20; 95% CI: 1.06, 1.36; P = 0.0004; I2 = 0%).
- Between ARI-A and BUP-A there was no significant difference in remission rates (RR: 1.05; 95% CI: 0.94, 1.17; P = 0.42; I2 = 33%)
- No significant difference was observed in adverse events and serious adverse events among the three treatment strategies.

Ji M, et al. PLoS One. 2024 Apr 26;19(4):e0299020.

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## Discussion

**Limitations**

I2 = heterogeneity (higher numbers = higher heterogeneity) which makes results difficult to apply.
Aripiprazole may not be the best antipsychotic medication for everyone.
Bupropion may not be the best antidepressant for everyone.

**Conclusions**

It is logical to initiate a medication that can produce a faster response when treating severe MDD.
It is still important to ensure the first-line/primary agent is efficacious, and rapid augmentation can cloud this assessment but may be necessary for the benefit of the patient.

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## 04

## Suicidality

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## Background

- May occur in patients experiencing MDD, other psychiatric diagnosis, or individuals with no psychiatric history.
- Suicide is defined as death caused by self-directed injurious behavior with intent to die as a result of the behavior.
- A suicide attempt is a non-fatal, self-directed, potentially injurious behavior with intent to die as a result of the behavior.
  - A suicide attempt might not result in injury.
- Suicidal ideation (SI) - thinking about, considering, or planning suicide.
- As of 2019, the Centers for Disease Control and Prevention listed suicide as the 10th leading cause of death among Americans (47,500 people)
  - 2nd leading cause of death among 10 to 34-year-olds
- All patients diagnosed with MDD should be assessed for suicidal thoughts
- Suicidality can be passive or active, and can fluctuate from moment to moment

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## Screening

- **Anyone with risk factors:**
  - Chronic major mental illness or personality disorders
  - History of previous suicide attempts or SUD
  - Chronic medical conditions or pain
  - Limited coping skills or ability to identify reasons for living
  - Unstable psychosocial support (housing, relationships, employment)
- **Tools**
  - Question # 9 of the PHQ-9
    - "Do you have thoughts that you would be better off dead or of hurting yourself in some way?"
  - Columbia-Suicide Severity Rating Scale (C-SSRS)
  - Suicide Assessment Five Step Evaluation and Triage (SAFE-T)
- **Cause? (MDD, life stressors, other psychiatric diagnosis)**

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

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## Warning signs

- Recognition of warning signs is the key
  - Helps create an opportunity for early assessment and intervention
- Three direct warning signs are particularly indicative of suicide risk:
  - Communicating suicidal thought verbally or in writing
  - Seeking access to lethal means such as firearms or medications; and
  - Demonstrating preparatory behaviors such as putting affairs in order
- Presence of one or more of these warning signs is a strong indication that further assessment is needed
- Indirect warning signs (e.g., agitation, hopelessness, insomnia, shame) are important to assess as well

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

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## Severity

- High Acute Risk
  - Plan
  - Means and/or access
  - Recent attempt
  - Inability to maintain safety
  - Acute episode related to psychiatric diagnosis
- C-SSRS screening version can help differentiate low, moderate, or high risk.

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

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## 05 Interventions

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## Nonpharmacological

- **Cognitive Behavioral Therapy**
- **Crisis Response Plan**
- **Reduced access to means**
  - Weapons
  - Time alone
  - Specific medications
  - Medication quantities
- **Increased outreach**
- **Case/care management**

NATIONAL SUICIDE PREVENTION LIFELINE 1-800-273-TALK (8255) suicidepreventionlifeline.org

CRISIS TEXT LINE | Text HELLO to 741741 Free, 24/7, Confidential

Veterans Crisis Line 1-800-273-8255 PRESS 1

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.

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## Pharmacological

- Medications to target underlying diagnosis
  - Could see multiple agents used
- Therapies with positive evidence for suicidality
  - Ketamine augmentation
    - IV 0.5 mg/kg has moderate evidence for acute symptom improvement of SI within 24 hours of treatment, with a moderate effect size that continues for 1-6 weeks.
    - In a meta-analysis of ketamine trials, 55% of patients after 24 hours and 60% at seven days reported no suicidal ideation.
  - Esketamine (not discussed in GL)
  - Lithium + additional psychotropic
  - Clozapine for schizophrenia or schizoaffective

VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. 2019.
Fan W, et al. Oncotarget. Jan 10 2017;8(2):2356-2360
Grunebaum MF, et al. Am J Psychiatry. Apr 1 2018;175(4):327-335.
Wilkinson ST, et al. Am J Psychiatry. Feb 1 2018;175(2):150-158.

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## Test your knowledge

A patient with a history of severe MDD presents for regular follow-up and discloses suicidality with a plan. Current medication include sertraline 200 mg by mouth daily. What is an appropriate intervention?

A. Initiate ketamine
B. Initiate lithium
C. Change sertraline to venlafaxine
D. Initiate CBT

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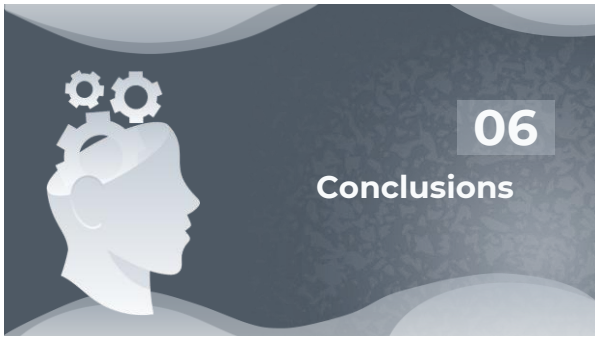


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## Take Home Points

- Severe depression describes the presentation and does not necessarily direct treatment decisions or outcomes.
- Number of symptoms, level of impairment of function, or PHQ-9 score can be used to gauge severity.
  - Modifiers for severity exist (SI, HI, psychosis, etc.)
- Nonpharmacologica interventions for suicide are strong (versus weak for drugs) recommendations.
- Must address and treat underlying problem successfully.
  - This includes treating insomnia.
- Lithium used to be the predominant medication for augmentation of suicidality, but ketamine is now recommended in the most recent guidelines.

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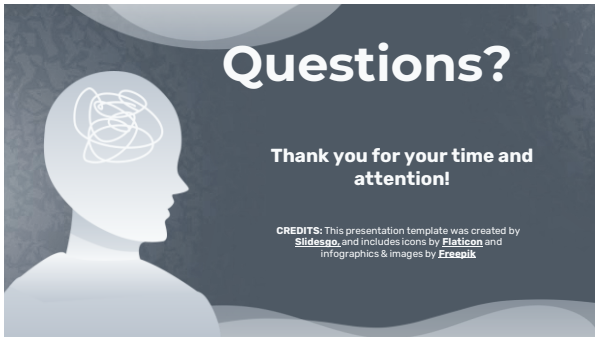


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